Invasive Paranasal and Pulmonary Aspergillosis in a Post-COVID Patient with Diabetes

Soumalya Pradhan, Srijita Karmakar, Souradeep Dutta
Intern, IQ City Medical College and Hospital, Durgapur, West Bengal, India

Abstract
COVID-positive patients and those recovering from COVID affliction are more susceptible to fungal infections. It is especially true in patients who are diabetic, on prolonged glucocorticoid medications and transplant patients. In critically ill patients, invasive fungal infections have a bad prognosis resulting in grim figures of morbidity. Glucocorticoid medications may aggravate hyperglycemia in patients with diabetes which present a favorable ground for fungal infections. In this case, we have come across a patient who has a long-standing history of diabetes. She has been suffering from invasive pulmonary aspergillosis while recovering from COVID-19. The diagnosis of invasive aspergillosis is difficult using clinical criteria, thus imaging modalities are the mainstay for diagnosis. Intravenous voriconazole (400 mg BD tapered down to 200 mg) has been used to treat her condition. Patients who are on glucocorticoids, have deteriorating pulmonary functions, and are diabetic have increased risk of developing aspergillosis.

Keywords: COVID-19, Diabetes, Fungal infection, Glucocorticoids, Invasive aspergillosis

INTRODUCTION
COVID-19, caused by betacoronavirus SARS-CoV-2 which originated in Wuhan, China, in 2019, has resulted in a global pandemic and cases have been skyrocketing ever since.[1] India especially has witnessed multiple waves of this deadly virus that has resulted in high mortality and morbidity.[2] Many fungal coinfections may be associated with patients with preexisting comorbidities like diabetes mellitus. Chronic hypertension, cardiac, and lung diseases aggravate the severity of this infection. India is presently the diabetic capital of the world, therefore, being on the precipice for developing complications.[3] Glucocorticoids have contributed to an immunocompromised state of the patients resulting in an increased number of invasive fungal infections. Here, we present a case of a diabetic woman recovering from COVID-19 who has developed invasive pulmonary and paranasal aspergillosis.

PRESENTATION OF CASE
A 64-year-old COVID-19-positive woman presented to the Emergency Department of IQ City Medical Hospital on May 23, 2021, with the chief complaint of a fall in the bathroom. On examination, she was breathless and had intermittent fever (>38.5°C).

She had a history of insulin-dependent type 2 diabetes mellitus and hypertension. She had tested COVID positive on May 14. She received the following medications: antihypertensives, proton-pump inhibitors, antipyretics, antibiotics, antihelminthics, glucocorticoids, zinc and multivitamin supplements, insulin injection, and nonsteroidal anti-inflammatory drugs.

Her partial pressure of O₂ was 96%, respiratory rate 22/min, temperature 98.6°F, arterial blood pressure 140/80 mmHg, pulse rate 70/min, and GCS 15. Hemoglobin was 10.2 g/dl, WBC total count 25.7 × 1000/μL, and C-reactive protein 395 mg/L.

The patient was shifted to the COVID isolation ward. Her CBG* level peaked up to 352 mg/dl

*CBG - Capillary Blood Glucose (Normal Level - Fasting 72–99 mg/dl, Postprandial – Up to 140 mg/dl). She was...

given injection human actrapid through subcutaneous route as a medication.

Chest X-ray PA View
It shows bilateral asymmetric interstitial and septal opacities [Figure 1].

Axial Section of CT Thorax
It revealed patchy areas of ground-glass haziness with vascular thickening noted in bilateral lung field – features are in keeping with atypical interstitial pneumonia – CORADS 5 [Figure 2].

CT scan of paranasal sinus with magnetic resonance imaging orbit screening revealed right-sided acute on chronic pansinusitis with rarefaction of bony walls along with small bony fenestration in the anteroinferior wall of the maxillary sinus with overlying soft-tissue inflammatory changes, air foci in the adjoining hard palate [Figure 3].

Additional extra paranasal sinus involvement is seen in the right intraorbital and periorbital space with edema and inflammation. There was associated orbital and periorbital cellulitis [Figures 4 and 5].

ECG findings revealed left ventricular hypertrophy with inferior wall ischemia.

She tested negative for COVID-19 on RTPCR on May 25 [Figure 6].

On further examination by an ophthalmologist, it was revealed that she had periorbital edema, orbital cellulitis, ecchymosis, and chemosis in the right eye [Figure 7]. Pupillary reactions were positive. History of dental infection was also elicited. She also had redness of the right cheek.

Figure 1: Bilateral asymmetric interstitial and septal opacities

Figure 2: Axial section of CT thorax: Multiple nodular lesions with a ground-glass halo are seen in both lung fields as shown by red arrow

Figure 3: Axial section of CT PNS: Right-sided maxillary sinusitis with rarefaction and thinning of the bony walls (arrow)

Figure 4: Axial section of CT PNS: Erosion in the anterior-inferior wall of the maxillary sinus was present. There was adjoining soft-tissue inflammatory changes in gingiva with intervening air lucencies (arrow)
On inspection of the oral cavity, there was a presence of blackish discoloration and erosion of the palate [Figure 8]. Scraping was done from all over the margins and center of the discoloration. It was sent for KOH mount and culture. She has suspected to have mucormycosis.

**Microbiological Finding**

The sample showed numerous thin hyphae with acute-angled branching [Figure 9 black arrow] and frequent septae [Figure 9 white arrow].

In this case, our microbiological finding was typical of the Ascomycetes family.

**DISCUSSION**

According to recent statistics, 8% of COVID-19 patients have developed fungal or other secondary infections during their hospital stay. There was no underlying evidence of infection, yet 72% of patients had received broad-spectrum antibiotics.[4] In an observational multicentric study conducted by clinicians in Bengaluru, India, it was seen that there is a relationship between SARS-CoV-2, corticosteroid administration, uncontrolled diabetes mellitus, and incidence of aggressive maxillofacial and rhino-cerebro-orbital fungal infections.[5]

The COVID-19 patients who have a cytokine storm develop inflammation in the lungs which may result in acute lung injury and damage to other organs which eventually leads to multiorgan failure. Steroids being one of the best anti-inflammatory drugs, COVID-19 patients are treated with it. Advocacy by NATIONAL CLINICAL MANAGEMENT PROTOCOL COVID-19 states that intravenous methylprednisolone 0.5–1 mg/kg/day should be administered for 3 days in moderate cases and 1–2 mg/kg/day in severe cases.[6] On the other hand, steroids also suppress the body’s immune system.[7] Hence, the body becomes more prone to developing a wide range of infections, especially fungal infections. In India, a huge

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**Figure 5:** MRI coronal STIR image of the patient shows diffuse intraconal fat stranding, as shown by the red arrow

**Figure 6:** MRI sagittal STIR image of the patient shows pre-maxillary inflammatory focus, as shown by the white arrow

**Figure 7:** Periorbital oedema, orbital cellulitis, ecchymosis and chemosis in the right eye

**Figure 8:** Blackish discoloration and erosion of the palate (Black arrow)
number of patients suffering or recovering from COVID-19 have been suffering from fungal infections resulting in high mortality and morbidity. While COVID-19-associated mucormycosis is increasingly recognized, invasive pulmonary and paranasal aspergillosis is not common. The global prevalence of aspergillosis was 5.4%.[8]

Here, in IQ City Medical College and Hospital, we have come across a patient who has a long-standing history of diabetes. She has been suffering from invasive pulmonary aspergillosis while recovering from COVID-19. Intravenous voriconazole (400 mg BD tapered down to 200 mg) has been prescribed. The signs of orbital cellulitis were discerned only after 4 days of admission to the hospital. In our case, a previously undiagnosed invasive pulmonary and paranasal aspergillosis infection may have been aggravated or it may have subsequently developed.

CONCLUSION

A significant increase in the incidence of both bacterial and fungal infections in COVID-19 is possibly due to immunosuppression. As the treatment protocol of COVID-19 includes the use of steroids, it has led to the development of opportunistic fungal diseases. Physicians should circumspect the possibility of invasive secondary fungal infections like aspergillosis in patients with COVID-19, especially in patients with preexisting risk factors. This report is a conscious effort to promulgate the significance of early detection and treatment of opportunistic infections. The most calamitous ones are SARS-CoV-2-associated mucormycosis and invasive pulmonary and paranasal aspergillosis. Hence, a due cognizance of this fact with a well thought out approach toward treatment may be able to reduce the morbidity and mortality associated with COVID-19 complications.

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